Clinical practice guidelines for the use of noninvasive positive-pressure ventilation and noninvasive continuous positive airway pressure in the acute care setting

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The full-text version of these guidelines is available at www.cmaj.ca

See related commentary by Bersten

Noninvasive ventilation is an important option in the management of patients who are at risk of or have respiratory failure in the acute care setting. Over the past two decades, the use of noninvasive positive-pressure ventilation and of noninvasive continuous positive airway pressure by mask has increased tremendously among acutely ill patients. Initial case series and uncontrolled cohort studies that suggested benefit in selected patients[1] led to many randomized controlled trials (RCTs).[1–3] Both methods of ventilation have been used to avoid endotracheal intubation in different patient populations with variable success.[1–3] In addition, noninvasive positive-pressure ventilation has been used to facilitate early liberation from conventional mechanical ventilation[4] and to prevent reintubation.[4]

Comprehensive guidelines on the use of noninvasive ventilation have been published previously.[7–9] Since then, the growing body of literature and variation in practice[5,6] have underscored the need for new clinical practice guidelines for the management of patients who have acute respiratory distress or failure. To develop these guidelines, we conducted a systematic and comprehensive review of RCTs in this area. We considered more recent literature (an additional 58 trials), included only evidence from RCTs and used GRADE methodology (Grading of Recommendations Assessment, Development and Evaluation)[10–12] to formulate the recommendations. Moreover, we have addressed the use of noninvasive ventilation in additional clinical settings: the postoperative setting, use for immunocompromised patients, weaning from conventional mechanical ventilation, transition to spontaneous breathing and the use for patients at high risk of respiratory failure after extubation.

Although these guidelines were developed in the context of the Canadian health care system, we considered RCTs from any country. Therefore, we believe that these recommendations are generalizable and useful to all clinicians who care for patients who are at risk of or who have acute respiratory distress or failure in an acute care setting.

Throughout this article, we include respiratory distress that is manifested by increased work of breathing but that does not meet traditional criteria for respiratory failure in our definition of acute respiratory failure. When we use the term "noninvasive ventilation," we are referring to noninvasive positive-pressure ventilation and continuous positive airway pressure. Finally, when we use the term "continuous positive airway pressure," the mode of delivery is understood to be by mask.

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Key points

- Noninvasive positive-pressure ventilation should be the first option for ventilatory support for patients with either a severe exacerbation of chronic obstructive pulmonary disease (COPD) or cardiogenic pulmonary edema.
- Continuous positive airway pressure delivered by mask appears to be equally effective to noninvasive positive-pressure ventilation for patients with cardiogenic pulmonary edema.
- Patients with acute respiratory distress or hypoxemia, either in the postoperative setting or in the presence of immunosuppression, can be considered for a trial of noninvasive positive-pressure ventilation.
- Patients with COPD can be considered for a trial of early extubation to noninvasive positive-pressure ventilation in centres with extensive experience in the use of noninvasive positive-pressure ventilation.

Methods

Leadership and scope

An 18-member guidelines panel of university-affiliated clinicians, led by two cochairs, was formed in June 2007 as an initiative of the Canadian Critical Care Trials Group / Canadian Critical Care Society Noninvasive Ventilation Guidelines Group. Of the 18 members on the panel, 16 participated in the review of RCTs, working in eight pairs. All 18 members of the panel were responsible for the literature review, quality appraisal, summary of the evidence, generation of the first draft of recommendations and revision of the recommendations.

These guidelines, set in the context of the Canadian health care system, are intended to help physicians make appropriate decisions regarding the use of noninvasive positive-pressure ventilation and continuous positive airway pressure in the following patient populations: patients who are at risk of or who have acute respiratory failure, postoperative patients and patients who are being weaned from mechanical ventilation or have recently undergone extubation.

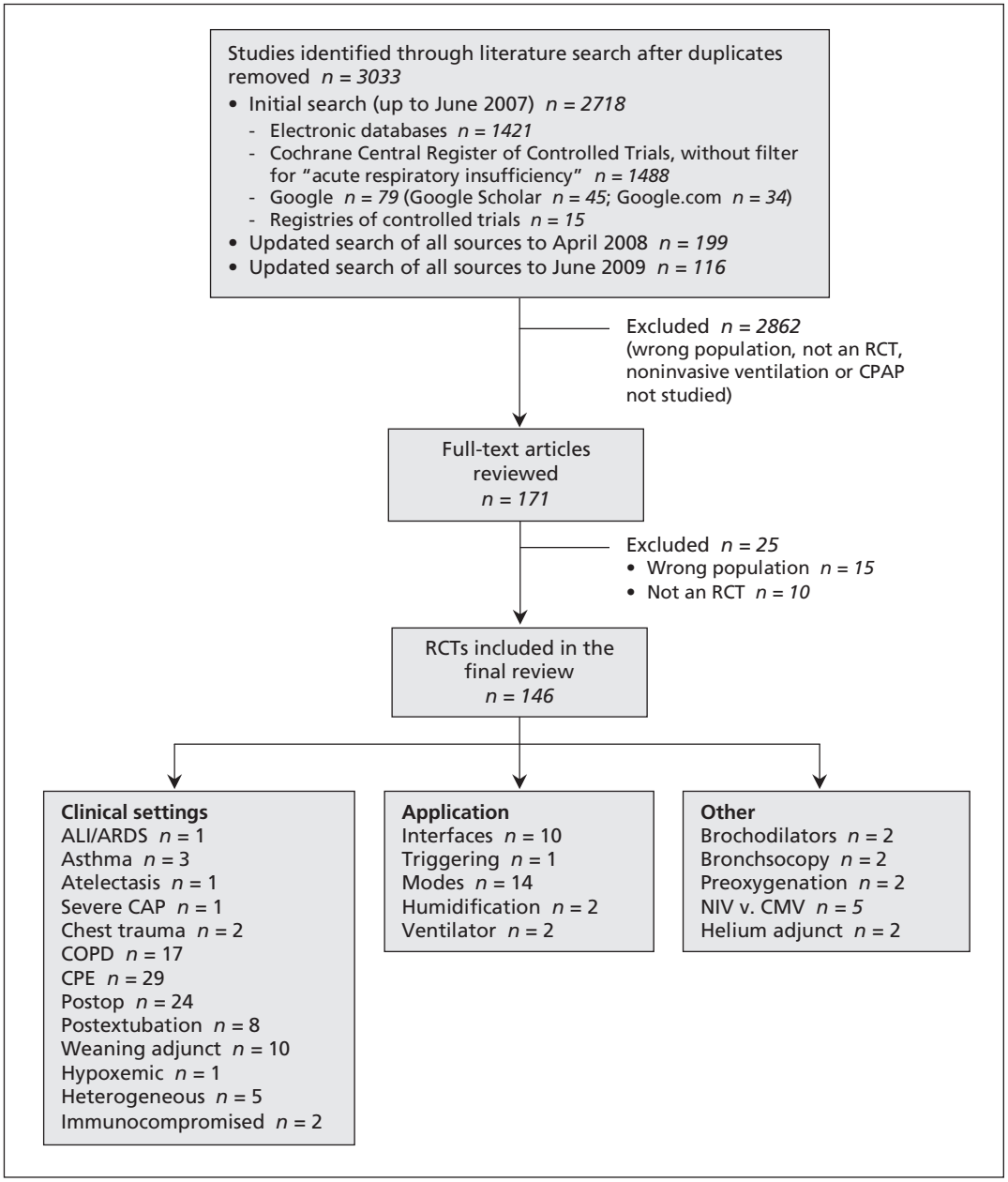

Figure 1: Summary of search results. ALI = acute lung injury, ARDS = acute respiratory distress syndrome, CAP = community-acquired pneumonia, CMV = conventional mechanical ventilation, COPD = chronic obstructive pulmonary disease, CPAP = continuous positive airway pressure, CPE = cardiogenic pulmonary edema, NIV = noninvasive ventilation, RCT = randomized controlled trial.

Literature review

We searched the following electronic databases from their inception to June 2009: MEDLINE, EMBASE, CINAHL, CENTRAL (the Cochrane Central Register of Controlled Trials), DARE (the Database of Abstracts of Reviews of Effectiveness), the Cochrane Database of Systematic Reviews, the ACP Journal Club database, the metaRegister of Controlled Trials, ClinicalTrials.gov and the Journals@Ovid database. We also searched personal files and the bibliographies of relevant articles. We identified RCTs that included adults admitted to hospital who were at risk of or who had acute respiratory failure. We included studies involving patients with acute or acute-on-chronic respiratory failure. No language restrictions were applied; non-English publications were translated into English.

Working independently, each member of the pair of reviewers critically appraised assigned RCTs. For each RCT, data were abstracted regarding trial validity. All reported outcomes were recorded. We conducted meta-analyses for topics for which at least two RCTs were identified.

A total of 146 RCTs were included in our review. Figure 1 provides a summary of the search results.

Development of recommendations

We used the GRADE approach[10–12] to develop the guideline statements. We incorporated assessments of study validity (using GRADE methodology), safety, feasibility and cost in developing our recommendations.

Table 1 summarizes the GRADE Working Group's definitions of its categories.[10–12] Standard phrases in these statements were "recommend," "suggest" or "no recommendation." For topics we considered to have sufficient quality and quantity of supporting evidence from RCTs, strong recommendations were assigned a grade of 1 and described by the phrase "we recommend"; weaker recommendations were assigned a grade of 2 and described by the phrase "we suggest." For topics that lacked sufficient evidence, we made no recommendation. In these situations, we stated that noninvasive positive-pressure ventilation or continuous positive airway pressure could be considered but that there was a lack of literature to support either intervention because published RCTs were inconclusive (denoted by the term "lack of sufficient evidence") or because no RCTs were published (denoted by "lack of RCTs").

The Canadian Critical Care Society and the Canadian Critical Care Trials Group reviewed the guidelines and endorsed the final version. In addition, an international expert on noninvasive ventilation reviewed the final guidelines.

Further details of the methods can be found in the full-text version of the article (available online at www.cmaj.ca).

Highlights of the guidelines

The complete list of guidelines organized by clinical group and grade of recommendation is in Table 2 of the full-text version (available at www.cmaj.ca). We defined three clinical settings: acute respiratory failure, weaning from mechanical ventilation and the postoperative setting. We also report recommendations on technical strategies to optimize the use of noninvasive ventilation (e.g., interfaces, mode). A summary of the recommendations, organized by strength and quality of evidence, is presented in Table 2 of this article.

The following are highlights of the key recommendations.

Which patients should receive a trial of noninvasive ventilation?

Noninvasive positive-pressure ventilation and continuous positive airway pressure are used most commonly in patients who have acute respiratory failure. The objective is to support the

Table 1: Summary of grading used in GRADE approach[10–12]

Numeric grade	Strength of recommendation	Interpretation
1	Strong	Do it Don't do it
2	Weak	Probably do it Probably don't do it
No grade	No recommendation (insufficient evidence)	Okay to try, an option
Letter grade	**Level of quality**	**Interpretation**
A	High	Further research is very unlikely to change our confidence in the estimate of effect
B	Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
C	Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
D	Very low	Any estimate of effect is very uncertain

Note: GRADE = Grading of Recommendations Assessment, Development and Evaluation.

work of breathing and improve oxygenation and ventilation while permitting other treatments (e.g., bronchodilators, antibiotics and diuretics) to reverse the underlying cause of the respiratory failure. The amount of literature available reflects the relative incidence of the underlying causes of respiratory failure.

Numerous RCTs supported the benefit of noninvasive positive-pressure ventilation in patients who have a severe exacerbation of chronic

Table 2: Guideline statements according to strength of recommendation and quality of evidence (part 1 of 2)

Grade/strength of recommendation (interpretation)	Level of quality (interpretation)	Statement
1A (Do it)	High	• We recommend the use of NPPV in addition to usual care in patients who have a severe exacerbation of COPD (pH < 7.35 and relative hypercarbia) • We recommend the use of either NPPV or CPAP in patients who have cardiogenic pulmonary edema and respiratory failure in the absence of shock or acute coronary syndrome requiring urgent coronary revascularization
1C (Don't do it)	Low	• We recommend that CPAP not be used in patients who have acute lung injury
2B (Probably do it)	Moderate	• We suggest that NPPV be used in immunosuppressed patients who have acute respiratory failure • We suggest that NPPV be used to facilitate early liberation from mechanical ventilation in patients who have COPD, but only in centres that have expertise in NPPV • We suggest that NPPV be used after planned extubation in patients who are considered to be at high risk of recurrent respiratory failure, but only in centres that have expertise in NPPV
2C (Probably do it)	Low	• We suggest that CPAP be used in patients who have respiratory failure after abdominal surgery • We suggest that NPPV be used in patients who have respiratory failure after lung-resection surgery • We suggest the use of an oronasal rather than a nasal mask in patients who have acute respiratory failure and who are receiving NPPV
2C (Probably don't do it)	Low	• We suggest that helium–oxygen (heliox) not be routinely used in patients who are receiving NPPV in the setting of a severe exacerbation of COPD • We suggest that NPPV not be used after planned extubation in patients who are considered to be at low risk of respiratory failure • We suggest that NPPV not be routinely used in patients who do not have COPD and who have postextubation respiratory failure
No grade (OK to try, an option)	Low (RCTs exist but findings inconclusive)	*NPPV or CPAP* • We make no recommendation about the use of either NPPV or CPAP in patients who have hypoxemia and who undergo bronchoscopy • We make no recommendation about the use of either NPPV or CPAP in low-risk patients after low-risk surgery to prevent respiratory failure • We make no recommendation about the use of either NPPV or CPAP in patients at high risk (because of associated comorbidity) to prevent respiratory failure after low-risk surgical procedures *NPPV* • We make no recommendation about the use of NPPV versus intubation and conventional mechanical ventilation in patients who have a severe exacerbation of COPD that requires ventilator support • We make no recommendation about the use of NPPV in patients who have an exacerbation of asthma • We make no recommendation about the use of NPPV in patients who have severe community-acquired pneumonia and no prior history of COPD • We make no recommendation about the use of NPPV to facilitate early liberation from mechanical ventilation in patients who do not have COPD • We make no recommendation about the use of NPPV in patients who have COPD and who have postextubation respiratory failure • We make no recommendation about the use of an oronasal mask versus full face mask for NPPV in patients who have acute respiratory failure

obstructive pulmonary disease (COPD) (references available in the full-text version of the article) or cardiogenic pulmonary edema (references available in the full-text version of the article); however, there was insufficient evidence for use in patients with most other causes of respiratory failure. Immunosuppressed patients who present with respiratory distress or failure appear to benefit from noninvasive positive-pressure ventilation.[13,14]

Table 2: Guideline statements according to strength of recommendation and quality of evidence (part 2 of 2)

Grade/strength of recommendation (interpretation)	Level of quality (interpretation)	Statement
No grade (OK to try, an option) – continued	Low (RCTs exist but findings inconclusive) – continued	• We make no recommendation about the use of proportional assist ventilation versus pressure support ventilation in patients who are receiving NPPV for acute respiratory failure *CPAP* • We make no recommendation about the use of CPAP in patients who have chest trauma and respiratory distress • We make no recommendation about the use of CPAP to prevent respiratory failure after cardiac surgery • We make no recommendation about the use of CPAP to prevent respiratory failure after high-risk surgical procedures
No grade (OK to try, an option)	Low (no RCTs)	*NPPV or CPAP* • We make no recommendation about the use of either NPPV or CPAP in patients who have chest trauma without respiratory distress *NPPV* • We make no recommendation about the use of NPPV in patients who have acute lung injury • We make no recommendation about the use of NPPV in patients who have chest trauma and respiratory distress • We make no recommendation about the use of NPPV to prevent respiratory failure after cardiac surgery • We make no recommendation about the use of NPPV to prevent respiratory failure after high-risk surgical procedures • We make no recommendation about the use of NPPV in patients who have respiratory failure after abdominal surgery *CPAP* • We make no recommendation about the use of CPAP in patients who have a severe exacerbation of COPD • We make no recommendation about the use of CPAP in patients who have a severe exacerbation of COPD that requires ventilator support • We make no recommendation about the use of helium–oxygen (heliox) in patients who are receiving CPAP in the setting of a severe exacerbation of COPD • We make no recommendation about the use of CPAP in patients who have an exacerbation of asthma • We make no recommendation about the use of CPAP in patients who have severe community-acquired pneumonia and no prior history of COPD • We make no recommendation about the use of CPAP in immunosuppressed patients who have respiratory failure • We make no recommendation about the use of CPAP to facilitate early liberation from mechanical ventilation • We make no recommendation about the use of CPAP after planned extubation • We make no recommendation about the use of CPAP in patients who have postextubation respiratory failure • We make no recommendation about the use of CPAP in patients who have respiratory failure after lung-resection surgery • We make no recommendation about the use of oronasal versus nasal or full face mask for patients who have acute respiratory failure and who are receiving CPAP

Note: COPD = chronic obstructive pulmonary disease, CPAP = continuous positive airway pressure (by mask), NPPV = noninvasive positive-pressure ventilation, RCT = randomized controlled trial.

Continuous positive airway pressure has been extensively studied for cardiogenic pulmonary edema but much less so in other settings.

- We recommend the use of noninvasive positive-pressure ventilation in addition to usual care in patients who have a severe exacerbation of COPD (pH < 7.35 and relative hypercarbia) (grade 1A recommendation).
- We recommend the use of either noninvasive positive-pressure ventilation or continuous positive airway pressure for patients who have respiratory failure due to cardiogenic pulmonary edema in the absence of shock or acute coronary syndrome requiring urgent coronary revascularization (grade 1A recommendation).
- We suggest that noninvasive positive-pressure ventilation be used for immunosuppressed patients who have acute respiratory failure (grade 2B recommendation).
- We recommend that continuous positive airway pressure not be used for patients who have acute lung injury (grade 1C recommendation).

Is there a role for noninvasive ventilation after intubation?

Noninvasive positive-pressure ventilation or continuous positive airway pressure can be used in three situations for patients who require mechanical ventilation. First, and perhaps most controversial, is the substitution of noninvasive positive-pressure ventilation for invasive ventilation in patients who still need ventilator support. Several small trials suggested that this approach benefits patients who have a severe exacerbation of COPD.[4] Second, use of noninvasive positive-pressure ventilation or continuous positive airway pressure may be considered to avoid reintubation if respiratory distress or failure develops within the first 48 hours after extubation. However, trials did not support routine use in this setting.[15,16] Third, recent trials suggested that clinicians identify patients who are at high risk of respiratory failure after extubation and use noninvasive positive-pressure ventilation as a bridge to spontaneous breathing, rather than waiting for respiratory distress or failure to develop after extubation.[17–19] The studies supporting the use of noninvasive positive-pressure ventilation in all of these settings were conducted in centres experienced in the use of this intervention.

- We suggest that noninvasive positive-pressure ventilation be used to facilitate early liberation from mechanical ventilation in patients who have COPD, but only in centres that have expertise in noninvasive positive-pressure ventilation (grade 2B recommendation).
- We suggest that noninvasive positive-pressure ventilation be used after planned extubation in patients considered at high risk of respiratory failure, but only in centres that have expertise in noninvasive positive-pressure ventilation (grade 2B recommendation).
- We suggest that noninvasive positive-pressure ventilation not be used after planned extubation in patients considered at low risk of respiratory failure (grade 2C recommendation).
- We suggest that noninvasive positive-pressure ventilation not be routinely used in patients who do not have COPD and who have postextubation respiratory failure (grade 2C recommendation).

Is there a role for noninvasive ventilation in the postoperative period?

Postoperative respiratory complications are common and are likely to occur in patients who have either premorbid respiratory disease or who have had surgery that affects respiratory mechanics and diaphragmatic function. The number of RCTs on the routine postoperative use of noninvasive positive-pressure ventilation or continuous positive airway pressure, or the application of either option for patients in whom respiratory distress or hypoxemia develops, is growing. Unfortunately, the literature to date has largely focused on short-term physiologic outcomes. Many studies of continuous positive airway pressure used it as part of a chest physiotherapy routine, applying it for only brief periods on a scheduled basis. As such, only a few recommendations can be made owing to insufficient evidence.

- We suggest the use of continuous positive airway pressure for patients who have respiratory failure after abdominal surgery (grade 2C recommendation).
- We suggest the use of noninvasive positive-pressure ventilation for patients who have respiratory failure after lung-resection surgery (grade 2C recommendation).

How can noninvasive ventilation be used optimally?

The technology to apply noninvasive positive-pressure ventilation and continuous positive airway pressure continues to evolve, with increasing choices in the type of interfaces and improvements in traditional interfaces. Either type of noninvasive ventilation can be applied using intensive care unit ventilators or units developed specifically for noninvasive ventilation. Different modes of ventilation for noninvasive positive-pressure ventilation are available, although pressure support remains the most commonly used. Most of the literature on interfaces or type of ven-

tilator consisted of bench studies (using an artificial lung), crossover studies that involved patients who were not sick or whose condition was stabilized on noninvasive positive-pressure ventilation, and RCTs that used physiologic outcomes or measures of patient comfort. As such, few recommendations could be made. Other interfaces (i.e., full face mask), ventilator modes (i.e., pressure support ventilation, proportional assist ventilation) and use of humidification should all be considered options. A concern with proportional assist ventilation is that lack of feasibility and cost may preclude its widespread use.

- We suggest the use of an oronasal rather than a nasal mask in patients who have acute respiratory failure and who are receiving noninvasive positive-pressure ventilation (grade 2C recommendation).
- We suggest that heliox (a helium–oxygen gas mixture) not be routinely used in patients who are receiving noninvasive positive-pressure ventilation in the setting of a severe exacerbation of COPD (grade 2C recommendation).

Knowledge gaps

There are several patient populations who have acute respiratory distress or failure for whom we could not make recommendations because of insufficient evidence, including patients with cystic fibrosis or pulmonary embolism and patients who decline intubation near or at the end of life. Because of ethical barriers and infeasible sample sizes needed for RCTs in some patient populations, future guidelines may need to make statements based on non-RCT evidence. Other areas we suggest for future research include the use of noninvasive ventilation for severe community-acquired pneumonia, asthma, acute lung injury and chest trauma, use for early liberation from mechanical ventilation, use after planned extubation and use in the postoperative setting. Important unresolved technical issues that require further research include the optimal ventilator, mode of ventilation, trigger, interface and level of humidification.

Implementation

Implementation of these guidelines may require clinician education, additional health care personnel, organizational change or additional resources (equipment or beds with cardiopulmonary monitoring) to ensure safe and appropriate application of noninvasive positive-pressure ventilation and continuous positive airway pressure. Timely endotracheal intubation may be required if noninvasive ventilation fails. Strategies for the implementation of these guidelines should be developed for each relevant clinician group (physicians in different clinical areas and with different levels of training and expertise, respiratory therapists and nurses).[20,21]

Updating

We plan to update this guideline every four years.

References

1. Mehta S, Hill NS. Noninvasive ventilation. *Am J Respir Crit Care Med* 2001;163:540-77.
2. Keenan SP, Mehta S. Noninvasive positive pressure ventilation for patients presenting with acute respiratory failure: the randomized controlled trials. *Respir Care* 2009;54:116-26.
3. Mehta S, Al-Hashim AK, Keenan SP. Noninvasive positive pressure ventilation in patients with acute cardiogenic pulmonary edema. *Respir Care* 2009;54:186-95.
4. Burns KE, Adhikari NK, Keenan SP, et al. Use of non-invasive ventilation to wean critically ill adults off invasive ventilation: meta-analysis and systematic review. *BMJ* 2009;338:b1574.
5. Demoule A, Girou E, Richard J, et al. Increased use of noninvasive ventilation in French intensive care units. *Intensive Care Med* 2006;32:1747-55.
6. Burns KE, Sinuff T, Adhikari NK, et al. Bilevel noninvasive pressure ventilation for acute respiratory failure: survey of Ontario practice. *Crit Care Med* 2005;33:1477-83.
7. British Thoracic Society. BTS guideline: noninvasive ventilation in acute respiratory failure. *Thorax* 2002;57:192-211.
8. Chawla R, Khilnani GC, Suri JC, et al. Guidelines for noninvasive ventilation in acute respiratory failure. *Indian J Crit Care Med* 2006;10:117-47.
9. Schönhofer B, Kuhlen R, Neumann P, et al. Non-invasive ventilation as treatment for acute respiratory insufficiency. Essentials from the new S3 guidelines [article in German]. *Anaesthetist* 2008;57:1091-102.
10. GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ* 2004;328:1-3.
11. Schunemann HJ, Jaeschke R, Cook DJ, et al. An official ATS statement: grading the quality of evidence and strength of recommendations in ATS guidelines and recommendations. *Am J Respir Crit Care Med* 2006;174:605-14.
12. Guyatt G, Gutterman D, Baumann MH, et al. Grading strength of recommendations and quality of evidence in clinical guidelines: report for an American College of Chest Physician Task Force. *Chest* 2006;129:174-81.
13. Antonelli M, Conti G, Bufi M, et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. *JAMA* 2000;283:235-41.
14. Hilbert G, Gruson D, Vargas F, et al. Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. *N Engl J Med* 2001;344:481-7.
15. Keenan SP, Powers C, McCormack DG, et al. Noninvasive positive-pressure ventilation for post-extubation respiratory distress: a randomized controlled trial. *JAMA* 2002;287:3238-44.
16. Esteban A, Ferguson ND, Frutos-Vivar F, et al. Non-invasive positive pressure ventilation does not prevent reintubation and may be harmful in patients with postextubation respiratory distress: results of a randomized controlled trial. *N Engl J Med* 2004;350:2452-60.
17. Ferrer M, Valencia M, Nicola JM, et al. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med* 2006;173:164-70.
18. Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med* 2005;33:2465-70.
19. Ferrer M, Sellares J, Valencia M, et al. Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorder: randomized controlled trial. *Lancet* 2009;374:1082-8.
20. Sinuff T, Cook DJ, Giacomini M, et al. Facilitating clinician adherence to guidelines in the intensive care unit: a multicenter, qualitative study. *Crit Care Med* 2007;35:2083-9.
21. Sinuff T, Kahnamoui K, Cook DJ, et al. Practice guidelines as multipurpose tools: a qualitative study of noninvasive ventilation. *Crit Care Med* 2007;35:776-82.

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Contributors: Sean Keenan and Tasnim Sinuff are joint first authors on this paper. They led the process of guideline development, performing initial and subsequent selection of trials for review, coordinating distribution of material for review and face-to-face meetings and leading manuscript writing and submission. All of the authors were involved in the conception and design of the guideline development project and took part in a review of the GRADE process of guideline development before meetings. All of the authors except for Deborah Cook and Peter Dodek were involved in reviewing and evaluating selected trials and presenting summaries of these trials at the meetings. All authors were involved in discussions of the literature presented and in drafting initial statements following the GRADE process during the meetings. All of the authors contributed to the writing and revising of the manuscript and approved the final version submitted for publication.

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